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Medical Monitoring: A Beneficial Remedy for Residents Living Near an Environmental Hazard Site

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Abstract

Objective—People living close to an environmental hazard site may suffer health harms from real or perceived contaminant exposures. In class-action litigation, medical monitoring is a potential remedy that has been allowed in some jurisdictions but not others. From 1952-1989 a U.S. Department of Energy (DOE) uranium metal plant near Fernald, Ohio, released ionizing radiation and uranium particulates into the surrounding community.

Methods—Settlement of litigation between nearby residents and the DOE resulted in an 18-year medical monitoring program (N=9775) which focused on general health promotion rather than effects of uranium.

Results—Participation was higher than projected; decreases in common risk factors (cholesterol and blood pressure) and deaths from cancer have been observed.

Conclusions—These data support the appropriateness of comprehensive medical monitoring as a remedy for people affected by defined sources of environmental contaminants.

From December, 1990 through 2008, the Fernald Medical Monitoring Program (FMMP) provided health screening and promotion services to 9775 persons who resided within close proximity to the Feed Material Production Center, a former uranium processing plant at Fernald, Ohio. The FMMP was a result of a class action lawsuit against National Lead of Ohio (NLO) and the U.S. Department of Energy (DOE) on behalf of persons who lived near the plant, and was the largest medical monitoring program created through class action litigation as a response to an environmental exposure. After eighteen years of operation, health outcomes of participants clearly demonstrate the benefits of the examination program. An extensive computerized database and biospecimen repository will provide research resources far into the future.

This paper will describe the history of the project, the design of the program, and health outcomes for the population examined, and the research resources. We believe that comprehensive medical monitoring, as described, benefits people who live near an environmental hazard site and is an effective and appropriate remedy in environmental contaminant-related class action lawsuits.

History

In the early 1950's, the U. S. Department of Energy built a nuclear fuel processing plant known as the Feed Material Production Center (FMPC), located on a 1,050 acre complex near rural Fernald, Ohio, seventeen miles northwest of Cincinnati (1). The FMPC was a U.S. government facility operated by private contractors under the supervision of the U.S. Atomic Energy Commission and later the U.S. Department of Energy (DOE). National Lead of Ohio Inc. was the main contractor, and operated the plant from 1951 until December 31, 1985. The primary function of the plant was to convert uranium feed materials, in the form of uranium ore and concentrates, into uranium metal. This uranium metal was then machined into fuel cores or targets for nuclear reactors, which were shipped to other DOE sites in the nuclear weapons complex. Recycled materials from other DOE sites were received at the FMPC and used as feed materials for production or processed for recovery of uranium and waste disposal. Manufacturing at the FMPC continued until its suspension in July, 1989. In addition, the FMPC also served as a storage site for radioactive and other hazardous waste material from other DOE sites (1). In 1991, the name of the facility was changed to the "Fernald Environmental Management Project" (FEMP) in order to reflect the change in mission from production to environmental "clean up" (2), which was completed on October 29, 2006 (3).

Contamination from the Fernald uranium foundry and machining operations first made national headlines in the mid-1980's when several news organizations ran features about the impact of plant operations on workers and the community (4). Citizens were outraged by the extent of the off-site contamination which included releases of uranium and related products into the air and ground and surface water. Because there was uncertainty about the quantity of environmental radioactive emissions from the plant, in 1990 the Centers for Disease Control (CDC) contracted with Radiological Assessments Corporation for dosimetry reconstruction – an assessment of radiation and uranium doses to members of the public who had lived near the FMPC (5). This group reported that from 1952--1989, 470,000 kilograms of uranium dust and 160,000 curies of radon-222 were released into the atmosphere, while 90,000 kilograms of uranium were released into surface water (1). Most airborne releases of uranium dust occurred prior to 1973. Radon emissions from radioactive waste storage silos continued until the vents of the domes covering the silos were sealed in 1979 (1).

Persons residing in the general area became aware that radioactive materials had been emitted into the proximal environment in 1984; emissions prior to that time had not been reflected in the published record (4). In January 1985, a class action lawsuit was filed by the citizens (plaintiffs) against National Lead of Ohio, Inc., which operated the plant at that time and its parent corporation, NL Industries, Inc., which guaranteed performance of the contract (6). The bases of the lawsuit were emotional distress and property value diminution. After a non-binding "summary jury trial", a technique used by judges to encourage settlements in which a jury is impaneled to hear a summary of the evidence in a case without actually hearing witnesses, the parties agreed to a settlement in which \$78 million was awarded to the class (6,7). The settlement had three components: payments to individuals for emotional distress, payments to land owners for decreases in the value of real property, and a fund to support a medical monitoring program and epidemiologic studies (6). The settlement and funds were supervised by three special masters (trustees) appointed by Hon. S. Arthur Spiegel, U.S. District Court Judge.

Following the settlement, the Fernald Trustees issued a Request for Proposals to area institutions to conduct the medical monitoring portion of the settlement. The RFP asked applicants to submit a budget for 1,000 examinations. Interest far exceeded initial

expectations. Ultimately, over 11,000 class members were approved to receive an examination and over 9,700 actually received one. The Trustees selected the University of Cincinnati to design and direct the Program and the Mercy Fairfield Hospital as the preferred site for examinations. The Children's Hospital of Cincinnati also became involved because some of those eligible for examinations were children.

The rationale for including medical monitoring as a legal remedy in this class action lawsuit was as follows. The nearby residents' emotional distress was related primarily to the *potential* for harmful health effects resulting from environmental releases. A medical monitoring program to identify disease if present or to reassure those found to be healthy was one way to mitigate the emotional distress suffered by class members. The settlement also included provisions for supporting epidemiological studies. The rationale for this was that epidemiological studies could clarify whether harmful health effects occurred or not, thereby mitigating the distress related to uncertainty (6). Inclusion of medical monitoring and epidemiological studies as remedies in class action lawsuits is relatively novel and not accepted in all jurisdictions. The Hastings Law Journal reported in 1992 that the FMMP was the largest community medical monitoring program created as a result of litigation (8). The authors of this paper believe that it continues to be the largest and most extensive such program.

The key design feature of the Program was that the examination was comprehensive – it was focused on conditions that had the most potential to improve subsequent health without regard to whether those conditions were potentially related to exposures to hazards from the Plant. The rationale for this was that the known health effects of exposures such as radiation or the metal toxicity of uranium (9) didn't have very effective treatments (e.g. – lung cancer, renal disease, interstitial pulmonary fibrosis). In contrast, regardless of what exposures may have occurred in this population, we were certain that the leading causes of death and disability in the participating population would be the same as the general population – coronary heart disease, common cancers, and stroke. The risk of death and disability from some of these common conditions is modifiable through the application of known screening practices and risk factor reduction. In short, the Program was focused on conditions with the most potential to affect future health rather than conditions potentially related to environmental exposures.

In legal terms, then, the potential remedy was indirect. We were not able to prevent or mitigate most health harms that might have occurred from exposures to radiation or uranium, but we hoped that health benefits related to health screening and promotion activities for common conditions would balance or offset those exposure-related harms that we could not mitigate.

Population

To be eligible for the Program, the Court determined that applicants had to have lived or worked within five miles of the outer boundary of the FMPC for any continuous two-year period between January 1, 1952 and December 18, 1984. This time span represents the period of production at the site prior to general public knowledge of the emissions. Those who had worked at the facility (employees of National Lead of Ohio, Inc. or National Lead Industries) were excluded from participation. A separate legal action on behalf of former workers at the plant has resulted in establishment of a second medical monitoring program for that group.

Recruitment for the Program began in 1990 when local media (television, radio, newspapers) were used to inform those eligible for the Program; 5,000 applications were submitted by the end of this first recruitment effort. Continuing recruitment efforts in 1991

including a mailing to all persons who applied for monetary benefits of the Fernald settlement resulted in an additional 6,000 applications being received. The recruitment effort received good support from a variety of local institutions. For example, commercial banks in the area agreed to maintain a supply of application forms and to provide the necessary notarization. After applicants were approved by the Fernald Settlement Fund Trustees, their contact information was sent to the FMMP and an examination appointment was offered.

It is difficult to estimate the actual size of the cohort of persons who lived in the proximity of the FMPC between the years 1952 to 1984 and who were potentially eligible to participate. The CDC Dosimetry Reconstruction Project estimated there were 45,631 persons living and working within a 10-kilometer radius from the site's center, a domain somewhat larger than the settlement-determined five-mile exposure domain, measured from the site perimeter, (which is roughly 8.5 kilometer from site center). The CDC reported a final median estimate of 45,631 (90% Credibility Interval of 40,240 to 53,224) for the 10 kilometer exposure domain (10). These data would suggest that the FMMP (N=9775) includes about one-fourth of the population eligible to participate.

Of the FMMP population, 3,507 have ever lived within the two-mile ring of the exposure domain (3.8 kilometers from the site center), or 47% of the CDC median estimate (7,508) for the slightly larger 4 kilometer radius area. It appears that participation rates were higher for people who lived or worked close to the plant than those who lived or worked farther away.

Exposure Profile of the FMMP Population

Extensive uranium dose reconstruction using methods developed by the CDC have demonstrated that over 60% of the FMMP participants had such minimal exposure to uranium and radon that their cumulative ionizing radiation exposure was less than 3.2% over lifetime background levels. For the US population, background ionizing radiation exposure is estimated to be 3.6 mSv per year or 288 mSv lifetime (80 years), but the range of individual exposure estimates is wide (1-10 mSv per year), depending primarily on geographic location (11). The maximum estimate of yearly exposure beyond background for this 60% FMMP sub-cohort is only 5.5 mSv, small compared to the variation in yearly background exposure. Lifetime cumulative exposure from the FMPC for this unexposed sub-group ranges from 0.0 to <0.25 Sv. For the exposed sub-cohort (other 40%), cumulative lifetime exposure from FMPC ranges (approximately) from 250 mSv (0.25 Sv) to over 3660 mSv (3.66 Sv).

Demographic Characteristics of Participants

Over the eighteen year tenure of the program, 9,775 persons, including 8,770 adults aged 18 years or older at the time of the initial examination, have enrolled. Median age at enrollment for adults was 43 years; very few were non-whites (Table 1). Twenty-six percent (21.7%) had family incomes below \$20,000 at the time of their first medical examination (most in 1990-1993) and 13.7% of the adults had not graduated from high school. Smoking history at enrollment was similar to other populations; 22.3% of the population were current smokers and 25.1% were former smokers. Members of the FMMP population who lived within the two-mile ring were slightly different on some demographic parameters; they had lower incomes (25.4% with incomes below \$20,000), were less likely to be high school graduates (18.1%), and were more likely to be current smokers (27.6%) (Table 1). The area closer to the plant contained more farms than the area beyond the two-mile radius.

FMMP Initial Medical Examination and Testing

Between September and November, 1990, 51 participants were examined in a pilot study of the proposed FMMP protocols. The full program of initial adult examinations began in December, 1990 and most were completed by December 1993; a limited number of persons (6%) have been permitted to enroll in the Program since that date. Upon enrollment, all persons signed a consent use of biospecimens and data in future research studies. The program has full Institutional Review Board approval from the University of Cincinnati IRB.

At the initial visit, each participant received a thorough physician-performed history and physical examination, and a wide range of diagnostic tests (Table 2). Supporting staff collected a detailed family history. Information about work history, hobbies, and other activities that might impact studies of environmental or radiation exposures was collected by a questionnaire filled out by the participant prior to the initial visit.

Ongoing Re-examination Program

Re-examinations initially were offered to participants at 3-year intervals. Beginning with the fourth cycle of re-examinations, the examination interval was shortened to every two years based in part on logistics and funding (numbers had decreased to the point that we could offer exams every two years) and in part on medical considerations, mimicking the 2-year examination interval of the Framingham Heart Study (12). During the 18-year life of the Program, there were a total of eight cycles of examinations including the initial examination.

The Program offered very little diagnostic follow-up testing for abnormalities found on screening tests – participants were referred to their own physicians for follow-up testing. There were two exceptions to this. First, diagnostic mammograms and ultrasounds were offered to women with abnormal mammograms because this was a fairly frequent occurrence and because we considered these tests to be a part of the initial screening process, not really follow-up. Repeat chest x-rays were offered at a six month interval is recommended by the radiologist. The second exception was a small fund to pay for selected follow-up tests for patients who couldn't afford or arrange follow-up. For example, a chest CT scan might be arranged for a participant without health insurance who had an abnormal chest x-ray.

Follow Up Protocol

Test results were reviewed immediately by a nurse upon receipt and participants were contacted by phone if there was a significant abnormality. Otherwise, results were communicated by mail. The FMMP physician who did the examination reviewed the results and with the assistance of Program staff, prepared a detailed three-page summary letter covering the results of the exam and recommendations regarding any abnormal test results, follow-up, health habits, and identified risk factors. After review by a nurse clinical quality assurance monitor, the letter, copies of the record from the history and physical examination, copies of all diagnostic test results, a satisfaction questionnaire, and risk factor-appropriate educational materials were mailed to the participant. Copies of all findings and test results were mailed also to any physicians identified by participants.

Three to six months after FMMP examinations, each participant's medical record was audited by one of the Program's clinical quality nurses to follow-up on abnormalities or risk factors. Participants were called to determine the outcome of further medical care. If no follow-up had occurred, the nurse re-educated the participant about the finding and the importance of follow-up and called again monthly until follow-up had occurred or the

participant asked her to stop calling. When follow-up indicated that a new cancer diagnosis had been made, pathology reports and related medical record information were obtained to verify the final diagnosis.

Significant diagnoses made as a result of a Program examination were catalogued into three groups: Major (such as cancer, diabetes, abdominal aortic aneurysm), Minor (inguinal hernias, cataracts), or Risk Factor (new diagnosis of hypertension or high cholesterol). Over the 41,930 examinations performed through May 30, 2008, the Program has been wholly or partially responsible for 1688 diagnoses of Major conditions; some categories are tabulated in Table 3.

Costs of Examinations

As noted, the settlement of the lawsuit resulted in a fund of \$78 million (6). Under supervision of District Court Judge Spiegel, the Trustees made an initial allocation of the fund into 3 parts: compensation for property value diminution, payment of emotional distress damages, and a fund to support the FMMP and future epidemiological studies. The Trustees' challenging task was to ensure that the settlement fund was spent completely without overspending. The property value diminution claims and initial payments for emotional distress were made concurrent with the first several years of operation of the FMMP. There were later re-allocations of remaining funds to both the FMMP and to a second emotional distress payment. How much to allocate between emotional distress payments and the FMMP was somewhat controversial – two Court hearings were held during the course of the Program during which the Judge heard arguments on both sides of the issue and made decisions, resulting in allocation of additional funds to the FMMP (13,14).

The Trustees paid for examinations on a cost plus 10% overhead basis. The Program was able to achieve significant discounts from normal charges for the laboratory tests and x-rays. However, the extensive quality assurance and follow-up program described herein, the dedicated examination office space, and the detailed coding and double data entry performed to support later epidemiological research were more expensive than would be typical for a doctor's office doing screening examinations. For example, the average cost of an initial examination was about \$800 in 1990. Of this expense, about 40% (\$326) was for direct examination costs, and about 60% (\$480) was for Program administration, quality assurance and follow-up. The direct costs of re-examinations were slightly less, but the other costs were similar, at least on a per-examination basis.

Questionnaires

All participants of the FMMP completed an extensive questionnaire at the time of the first examination, requesting information about lifestyle risk factors, location of residences and drinking water sources, and information relevant to exposure via various pathways. Each year participants were asked to provide information about new medical problems and the names of the physicians who treated them, and hospitalizations or surgeries, including the health care facilities where care was received. The first questionnaire included the Health Risk Appraisal question set, with 60 items, originally developed by CDC and modified by the Carter Center and the University of Michigan Health Management Research Center (15). Yearly questions also asked about smoking (American Thoracic Society question set, (16) and alcohol use, diagnostic imaging, influenza vaccinations, and included the SF-36 health perception instrument (17). In addition to standard questions repeated each year, participants also were asked sets of special questions at each cycle, eliciting information about family history of cancer, physical activity, histories of sunburns and skin moles, female reproductive history and use of oral contraceptives, and breast feeding. Complete

reproductive history information was obtained from both males and females, and yearly pregnancy update questionnaires were sent to all female participants of child-bearing age. Questionnaire data collection was designed so that a different version of the form was sent to those who skipped a year of questionnaire return, covering multiple years of medical history experience. Through 2006, 83,928 completed questionnaires from adults had been received by the Program.

Continuing Participation

Yearly questionnaire return rates varied by Program year, but in 2006 was 59% of the original enrollees. Continued participation in the examination component Program fell 23% at the first re-exam for adults and has leveled off at about 50% for each examination cycle since then. Some participants skip one exam but then return for the next one. Only 216 participants have withdrawn from the Program and are no longer contacted or followed (except to obtain information when we learn of their death); 184 participants have been lost to follow-up. Thus, over 50% of initial participants still get semi-annual examinations and complete annual questionnaires and we know the location and vital status of 97% of the initial participants. Death certificates have been obtained, or an NDI search completed, on most of the 900 participants who have died.

Data Coding, Editing, and Computerization

Participants' records are standardized (edited and coded) under procedures designed by the program's epidemiologist. All diagnoses obtained by medical history interview and physical examination are coded by Accredited Record Technicians employed by the FMMP who work on-site at the medical monitoring program office, using International Classification of Disease (ICD) codes, Ninth Revision. Verification of accuracy of all ICD codes is performed by examination of a computer generated report listing both physician notation and translation of the code.

All information in the chart (medical examination findings, laboratory tests, diagnostic test results, questionnaire information) was double data entered into a relational SAS database with verification using SAS Compare. In addition, various computer-generated quality assurance reports are used for follow-up and to detect data outliers, which are then verified with the paper chart and the laboratory, if needed. All self-reported medication information was reviewed by program staff and then coded by type of drug using a 4-digit code. Diagnosis counts and code lists are available on the program website www.genmed.uc.edu/fmmp (18).

Program Oversight

A Citizens' Advisory Committee, consisting of the FMMP leadership, the plaintiff's attorney for the Class, and 3 – 5 citizen volunteers meets several times each year to review data on participation and medical outcomes and to discuss proposed changes to the Program. The Committee also reviews applications for access to the database and biospecimens for various research studies and submits a recommendation to the medical Director and Trustee who make the final decision. In addition, the Program Director sends quarterly progress reports to the Trustees, and attends Federal Court hearings on the settlement activities.

Data and Biospecimen Sharing

An extensive collection of archived samples, many collected as early as 1991-1993 and currently in excellent condition, exists and is available for studies of proteomics, genetic variation, and serum and urinary biomarkers of both exposure and disease. Samples of whole blood, serum, plasma and urine were obtained from all participants at the time of the

initial examination, and whole blood and serum were obtained in 2007-20. Written policies about access and the application forms are available on the FMMP website (18). With recommendations of the Citizens Advisory Group, the Court-appointed Trustee has approved 50 requests for access to data so far, resulting in 15 publications to date. The Citizens' Advisory Committee is particularly interested in encouraging research on the health effects of low-level radiation and uranium exposure. However, they are open to research questions of broader health significance, not related to exposure, and have approved access to the database and samples for such projects. The Trustee and the supervising federal judge also share a commitment to use of the database and biospecimens for high-quality research.

Outcomes

This report summarizes the first sixteen years of Program operation (1990 – 2006), as data entry for the last two years is not yet complete.

Health Benefits for the Participant Population

By the end of the 7th examination cycle, in November, 2006, a total of 1688 “Major” findings had been made *as a result of* the FMMP examination (Table 3). The most common “Major” finding was diabetes (486 cases). Others include 229 skin cancers, 145 breast cancers, 107 prostate cancers, 41 colon cancers, 38 lung cancers, and 37 urinary system cancers diagnosed as a result of examination findings. There were 8 cases of leukemia and 7 cases of lymphoma diagnosed as a result of the Program. Follow-up for the eighth examination cycle is not yet complete. In addition to diagnosis made as a direct result of a screening finding of the FMMP examination, between exams other diagnoses were made unrelated to this examination. However, the FMMP screening was responsible a significant portion of all cancer diagnoses, such as 145 of the 175 total breast cancer diagnoses.

Evidence of health benefits beyond individual anecdotal reports includes both mortality and risk factor data. SMR's have been calculated using the mortality data from the FMMP for different time intervals through 2004, and compared with the U.S. population (white race only, Table 4) (19,20). An SMR of 1.00 indicates that the mortality experience of the population of interest (e.g. - FMMP) is the same as the general population; values less than 1.00 mean less mortality. Among those who enrolled in the FMMP as adults (N=8758) life table analysis predicted 947 expected deaths (11%) by 2004, but, in fact, only 705 participants (8%) died. In other words, as of 2004, 242 more adult participants were alive than would have been predicted from general population statistics. There were 84 fewer cancer deaths than predicted.

Evidence that the observed mortality benefit has accrued over the tenure of the program includes a series of Standardized Mortality Ratios (SMR's) analyses (Table 4). At the end of the enrollment period in 1994, the 111 deaths that had occurred in the first 3 years of follow-up resulted in SMR's of 0.66 for all causes, 0.64 for all cancers, and 0.73 for all cardiovascular disease. These early, low SMR's are evidence that the FMMP population exhibited a “healthy volunteer effect” typical of cohort studies involving volunteers. Those who were already ill and seeing physicians regularly during the enrollment period and were probably less likely to enroll. It should be noted that the rate of current smoking (23%) at the time of the initial examination was almost identical to the Behavioral Risk Factor Surveillance System (BRFSS) rate for the southwest Ohio region (24%) for the same time period (21) suggesting that the FMMP population was similar to the general population on that risk factor.

When all deaths through 1996 were considered (213 deaths) the SMR's for all three categories increased slightly (0.72 for all causes, 0.77 for all cancers, and 0.75 for all cardiovascular) although each was still much below the general population mortality experience. The most recent calculations, through 2004 (705 deaths), show a decrease in SMR's from 1996 for all cancers (0.70, 95% CI 0.53, 0.95) and for all cardiovascular disease (0.69, 95% CI 0.57, 1.01) relative to the 1996 statistics. These decreases in SMR's with longer Program tenure, given the Program's excellent vital status ascertainment, would indicate that the Program improved survival, especially for the medical conditions for which there is extensive screening and follow-up (cardiovascular risk factors and cancer screening).

In addition to mortality, we have evidence of improvements in cardiovascular risk factor levels that should, with time, result in less heart and other cardiovascular diseases. In adult males who came to at least five of the first seven exams offered, mean total serum cholesterol levels decreased about 30 mg/dL, across almost all age groups (age group assignment based on age at each exam, Figure 1). The same cholesterol finding was noted in women age >55 years. In those who were regular participants, mean systolic blood pressure decreased about 5 mm/Hg in males from first exam to seventh exam, across all age groups >50 years. The introduction of cholesterol-lowering medications occurred in 1987, prior to the start of the Fernald Medical Monitoring Program. The decrease in serum cholesterol in consistent participants of the FMMP was greater than what has been reported for the general population over approximately the same time period. Serum cholesterol data from the NHANES studies conducted in 1988-1994 and in 1999-2002 indicate that for all adults aged 20 years or older, total serum cholesterol level dropped 3 mg/dL; for males 60-74 years, -10 mg/dL and females 60-74 years, 12 mg/dL (22). There was a small decrease in diastolic blood pressure for males and females during these intervals.

Value of the FMMP as a Resource for Research

The database and archived biospecimens represent a rich resource for future research of both health effects related to environmental exposure, and a wide range of non-exposure research questions, especially those of screening efficacy and predictors of future disease (23). The cohort contains both persons exposed to radiation and uranium and others who were not exposed beyond background levels. Extensive disease risk factor information has been collected and much of this information predates subsequent disease diagnosis.

The extensive coding of the medical information on this large cohort provides the immediate opportunity to ask specific research questions. For example, all of the 31,083 mammogram reports and the 27,855 chest x-ray reports in the database have been literally coded (coding of phrases) using a list of over 200 3-digit codes, specific to each type of imaging. Risk factor matrices have been developed from questionnaire information, such as a matrix of cumulative cigarette pack-years for all participants, for each calendar year. We also have matrices for family history of each type of cancer for each Program participant, with number of first degree and total number of blood relatives with that type of cancer.

The FMMP has repeat laboratory measures on blood, serum and urine analytes on all participants. A Medical Heritage program has been implemented to standardize the data for time and method-dependent changes. Not only has this program performed quality assurance by using such measures as 30 day moving averages of the healthy Fernald participants, we have established that it is possible to track laboratory data for each analyte in a manner that will allow for adjustment for possible laboratory analytical drift found in any prospective study (24). The FMMP Medical Heritage Program was able to detect an error in the lyophilized standardizing reagent distributed by NTIS for glucose, which was then reported in the literature (25).

We have collected family structure information from all participants through several types of questionnaires (family history at the time of the medial examination, questions about who else lived with you, and questions about offspring on one of the yearly questionnaires). In each instance, we have recorded names of these relatives and coded each mentioned family member with their FMMP ID if they are Program participants. With each questionnaire, we also ask participants the names of three personal contacts, and record their relationship to the Program participants. Using these multiple sources of information, we have created a family relationship database, which can be used to determine which participants are blood-relatives (and not statistically independent), and also to create family pedigrees and document degree of relatedness. There are 2415 known mother-child pairs, 1792 father-child pairs, and 2605 sibling pairs

Discussion

What is the appropriate remedy for a population of thousands of people exposed unwillingly to potentially dangerous environmental hazards? Money is an obvious answer yet money, by itself, seems so inadequate. The presumed potential harms are diseases related to those exposures. The ideal remedy, then, would be something that prevents or treats hazard-related diseases, yet many such diseases aren't fully preventable or even treatable once exposures have occurred. The next best option, then, is a program that strives to improve the health status of the affected population so that program-mediated improvements in health will offset whatever hazard-related harms have occurred. Despite this logic, medical monitoring programs such as the one described in this paper are not widely accepted across all jurisdictions as appropriate or allowable remedies in class action or other lawsuits involving environmental contaminants (26). We believe that the early findings of the Fernald Medical Monitoring Program described herein offer convincing evidence that a health screening and health promotion program as described can have significant and measurable health benefits to offset the potential health harms of environmental contaminants.

A purpose of this report is to publicize the availability of the research resources created by the foresight of the Court, the Settlement Fund Trustees, the plaintiffs' attorneys, and the community activists. What has been created here, in effect, is a cohort similar to the original Framingham cohort. The availability of frozen biological samples from the beginning of the Program (1990 – 93) for many of the participants adds to the potential value of the database. While this research resource may be valuable for almost any epidemiological inquiry, it is a particularly valuable database for research into the health effects of low-level radiation in the form of uranium dust and radon gas, and exposure to uranium metal. Most of what we think we know about health effects of radiation comes from extrapolation from relatively acute, high-dose exposures. This database and collection of biological samples offers a unique opportunity to study chronic, low level exposures to these hazards.

The principal limitation of the health benefits data reported is the fact that the cohort of individuals studied was a volunteer population. Thus, whether the health benefits observed were due to the Program interventions or were simply the result of attracting a healthier-than-average population may be argued. Our data support the notion of a “healthy volunteer” effect but also offer evidence of benefits in excess of the volunteer effect. In addition, the health screening and promotion measures employed by this project were, for the most part, measures proven to improve health or decrease morbidity and mortality. For example, regular use of screening mammography has been proven to reduce breast cancer mortality for women 50 years of age and over (27,28). The essence of this Program was to increase the use of these proven health improvement strategies. Thus, there is a plausible “biological mechanism” to support the epidemiological observations of fewer deaths and improved risk factor profiles.

In summary, we have provided a description of one of the first and probably the largest medical monitoring programs related to an environmental hazard site funded by proceeds of a class action lawsuit. Our results demonstrate that such monitoring can be a very effective legal remedy by providing general health benefits to balance potential harms that could result from environmental contaminants. In addition, because the data from almost 18 years of examinations have been coded and computerized, and because of the availability of frozen blood and urine samples from 1990-93, this Program is available to serve as a major resource for the study of the health effects of low-level radiation, uranium exposure and related issues.

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Serum Cholesterol Males: at least 5 Exams of the first 7 Exams

Figure 1. Total serum cholesterol of male participants in the Fernald Medical Monitoring Program, who participated in at least five of the first seven examinations

Table 1
Demographic Characteristics of Fernald Medical Monitoring Program Participants

	All	Ever lived within 2 miles of site ¹	Lived 3-5 miles from site ^{2,3}
Population	9775	4171	4848
Age at Enrollment			
< 18 years	997 (10.2%)	416 (10.0%)	532 (11.0%)
18-65 years	7905 (80.9%)	3443 (82.6%)	3850 (79.4%)
> 65 years	873 (8.9%)	312 (7.5%)	466 (9.6%)
Age (years) in 2007			
Median	56.0	55.0	56.0
Mean (sd)	56.4 (17.0)	55.8 (16.5)	56.3 (17.5)
Deceased as of 10/1/2007			
Male	476 (4.9%)	190 (4.6%)	231 (4.8%)
Female	424 (4.3%)	191 (4.6%)	210 (4.3%)
Race			
White	9715 (99.4%)	4154 (99.59%)	4828 (99.6%)
Black	16 (0.2%)	3 (.07%)	4 (0.1%)
Native American	13 (0.1%)	6 (.14%)	6 (0.1%)
Hispanic	6 (0.1%)	2 (.05%)	2 (0.0%)
Other	17 (0.2%)	6 (.14%)	8 (0.2%)
Income in 1991-93⁴			
< \$20,000	2120 (21.7%)	1649 (25.4%)	942 (19.4%)
>\$50,000	1951 (20.0%)	690 (16.6%)	1041 (21.5%)
Education⁴			
< HS Grad	1338 (13.7%)	1202 (18.1%)	503 (10.4%)
College grad	1181 (12.1%)	382 (4.0%)	700 (14.4%)
Smoking history at enrollment⁴			
Current	1997 (22.3%)	1051 (27.6%)	805 (18.1%)
Former	2247 (25.1%)	896 (23.5%)	1134 (25.5%)
Never	4715 (52.6%)	1860 (48.9%)	2509 (56.4%)

¹ Participants who lived within two miles of the plant at some time between 1952 and 1984.

² Participants who never lived within two miles of the site, but did live 3-5 miles from the site at some point between 1952 and 1984.

³ Some persons were eligible for the FMMP because of having worked within the exposure domain for at least 2 continuous years, but were not workers at the Fernald site. They are included in neither the group that ever lived within two miles nor in the group that lived 3-5 miles from the site.

⁴ Only includes participants who were adults at the time of enrollment; information on education, income and smoking were not collected from children at the time of enrollment.

Physician Examination Components

Table 2

Diagnostic Tests	Initial Exam	Follow-Up Exams	Lab Tests	Test Name	Initial Exam	Follow-Up Exams	Lab Tests	Test Name	Initial Exam	Follow-Up Exams
Chest X-Ray	X	3,4,5,6,7	Lipid Profile	Triglyceride	X	All	Thyroid	T4	X	T4 for 3 ⁶
Mammogram	X	Annually ¹		Cholesterol	X	All		TSH		3 ⁶ , 4, 5, 6, 7, 8
EKG	X	4,5,6,7,8		LDL (calc)	X	All				
Pulmonary Spirometry	X			HDL Chol	X	All	Diagnostic Immunology	Serum Beta-2 Microglobulin serum	X	Special ⁷
Flexible sigmoidoscopy	X	3,4	Hematology	CBC	X	All				
Stool-Occult Blood	X	All		White cell Differential	X	All	Urine	Urinalysis	X	All ⁸
Pap Smear	X	All 2						Urine Microalbumin	X	7
Vision Test		4,5,6,7,8	Chemistry	Serum Chemistry	X	All		Urine Beta-2 Microglobulin-urine	X	7; all ⁹
Hearing Test		4,5,6,7,8		Hemoglobin A1C		Special ⁴				
Blood and Urine for Cryopreservation	X	8 ³		PSA		All ⁵				

¹ Mammograms offered to all females age >=40 years.

² Vaginal pap smear obtained on all females age >=18 years.

³ At 7th exam, whole blood cytopreserved on all with a cancer diagnosis; at 8th exam, whole blood and serum cytopreserved on all participants.

⁴ Hemoglobin A1C measurement done on all with a plasma glucose >=126 mg/dl or known diabetic.

⁵ PSA done on all males age >= 50 starting with 2nd exam (1994).

⁶ Midway during the third exam cycle the program convert from doing T4s to TSHs because of cost and improved clinical value.

⁷ Serum B2M measured only on those with a urine B2M > 250 ug/L.

⁸ For exams 2, 3, 4,5,6, and 7, urine microscopic examinations were done only for those >45 years or with a history of blood in the urine. In exam 8, microscopic exams of urine were done on all participants.

⁹ After the first exam, urine B2M measured only if elevated at first exam; measured on all participants at 7th exam.

Table 3
Major findings discovered as a result of the Fernald Medical Monitoring Program

Finding	1 st Exam	2 nd Exam	3 rd Exam	4 th Exam	5 th Exam	6 th Exam	7 th Exam	Total [/]
Cancers								
Breast Cancer	29	20	16	20	22	19	19	145
Prostate Cancer	12	20	26	15	8	11	15	107
Lung Cancer	12	5	5	5	4	1	6	38
Colon Cancer	12	9	10	5	3	2	0	41
Skin Cancer	62	48	37	29	18	6	29	229
Significant Findings								
Chronic Lung	89	9	23	15	7	4	4	151
Diabetes	170	102	65	43	29	41	36	486
Gynecological	40	19	13	6	1	1	3	83

[/] Total number of significant findings over 7 exam cycles; follow-up for the 8th exam cycle is not yet complete.

Table 4
Standardized mortality ratios for the Fernald Medical Monitoring Program cohort, at 3 to 14 year intervals since the inception of the Program

	Standardized Mortality Ratio						
Cause of Death	Study End Date						
	1994	1996	1998	2000	2002	2004	
<i>No of Deaths</i>	111	213	316	413	563	705	
	12/31/1994	12/31/1996	12/31/1998	12/31/2000	12/31/2002	12/31/2004	
All Causes	0.66	0.72	0.72	0.69	0.73	0.74	
All Cancers	0.64	0.77	0.75	0.67	0.68	0.70	
All Cardiovascular	0.73	0.75	0.70	0.63	0.62	0.69	
Diabetes Mellitus	0.00	0.13	0.34	0.25	0.34	0.27	
Breast Cancer	1.08	1.15	0.80	0.60	0.69	0.66	
Prostate Cancer	0.41	0.48	0.49	0.47	0.36	0.66	
Lung Cancer	0.37	0.53	0.53	0.49	0.54	0.51	
Colorectal Cancer	0.39	0.45	0.70	0.63	0.58	0.66	